

## SEQUENCE LISTING

<110> Dunstan, Colin R.

<120> COMPOSITIONS AND METHODS FOR THE PREVENTION OR TREATMENT OF CANCER AND BONE LOSS ASSOCIATED WITH CANCER

<130> A-605

<140> 09/389,545

<141> 1999-09-03

<160> 8

<170> PatentIn Ver. 2.1

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Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
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Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln 65 70 75 80

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
85 90 95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
100 105 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
115 120 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser 15À Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe 20/0 Ser Cys Ser Val Met His Glu Ala\Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys <210> 2 <211> 401 <212> PRT <213> Human

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Pro Glu Thr Gly His Gln Leu Leu Cys Asp Lys Cys Ala Pro Gly Thr 

Tyr Leu Lys Gln His Cys Thr Val Arg Arg Lys Thr Leu Cys Val Pro 

Cys Pro Asp His Ser Tyr Thr Asp Ser Trp His Thr\Ser Asp Glu Cys 

Val Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Ser Val Lys Gln Glu 

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Glu Glu Gly Arg Tyr 

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Ser Gly Val Val Gln Ala Ġly Thr Pro Glu Arg Asn Thr Val Cys Lys Cys Pro Asp Gly Phe Phe\Ser Gly Glu Thr Ser Ser Lys Ala Pro Cys Ile Lys His Thr Asn Cys Set Thr Phe Gly Leu Leu Ile Gln Lys Gly Asn Ala Thr His Asp Asn Val Cys Ser Gly Asn Arg Glu Ala Thr Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg Phe Ala Val Pro Thr Lys Ile Ile Pro Asn Trp Leu Ser Val Leu Val Asp Ser Leu Pro Gly Thr Lys Val Asn\ Ala Glu Ser Val Glu Arg Ile Lys Arg Arg His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu 25/0 Trp Lys His Gln Asn Arg Asp Gln Glu Met\Val Lys Lys Ile Ile Gln 

Asp Ile Asp Leu Cys Glu Ser Ser Val Gln Atg His Leu Gly His Ser 

Asn Leu Thr Thr Glu Gln Leu Leu Ala Leu Met Glu Ser Leu Pro Gly 

Lys Lys Ile Ser Pro Glu Glu Ile Glu Arg Thr Atg Lys Thr Cys Lys 

Ser Ser Glu Gln Leu Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn 

Gly Asp Gln Asp Thr Leu Lys Gly Leu Met Tyr Ala Leu Lys His Leu 

Lys Thr Ser His Phe Pro Lys Thr Val Thr His Ser Leu Arg Lys Thr 

Met Arg Phe Leu His Ser Phe Thr Met Tyr Arg Leu Tyr Gln Lys Leu Phe Leu Glu Met Ile Cly Asn Gln Val Gln Ser Val Lys Ile Ser Cys Leu <210> 3 <211> 407 <212> PRT <213> Human <400> 3 Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro\Pro Gly Thr Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp\Glu Cys Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Ard Tyr Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly the Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys Arg Lys His Thr Asn 

Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr Gln Lys Ala Ala Ala

Cys Ser Val Phe Gly Leu Leu Thr Gln Lys Gl $\chi$  Asn Ala Thr His

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr\Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr I↓le Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser 33/0 Asp Ile Ala Val Glu Trp Glu Ser Asn Gly\Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn Hils Tyr Thr Gln Lys 

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Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys Leu Tyr Cys Ser Pro 

Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu Cys Asn Arg Thr His 

Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr Leu Glu Ile Glu Phe 

Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe Gly Val Val Gln Ala 

Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg Cys Pro Asp Gly Phe 

Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys Arg Lys His Thr Asn 

Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Ly's Gly Asn Ala Thr His 155<sup>\</sup> 

Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr C\(\)In Lys Cys Gly Ile 

Asp Val Thr Ala Ala Ala Glu Pro Lys Ser Cys Asp\Lys Thr His Thr 

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pto Ser Val Phe 

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser\Arg Thr Pro 

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pto Glu Val

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr

Lys Pro Arg Glu Glu  $\$  Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val 260  $\$  265 270

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
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Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser 290 295 300

Lys Ala Lys Gly Gln Pro Ard Glu Pro Gln Val Tyr Thr Leu Pro Pro 305 310 315 320

Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
325 330 335

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly 340 350

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp 365

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp 370 380

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His 385 390 400

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
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Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr 290 295 300 Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr 305 31À 315 Cvs Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu 325 330 Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu 340 345 Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys 3 6/0 355 Ser Arg Trp Gln Gln Gly Asn Val\Phe Ser Cys Ser Val Met His Glu 370 375 380 Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly 385 390 395 400 <210> 6 <211> 406 <212> PRT <213> Human <400> 6 Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp Glu Glu Thr Ser His 15 1 5 10 Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr Tyr Leu Lys Gln His 30 20 Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro Cys Pro Asp His Tyr

Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys Leu Tyr Cys Ser Pro
50 55 60

Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu Cys Asn Arg Thr His
65 70 75 80

Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr Leu Glu Ile Olu Phe
85 90 95

Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn\Thr Val Cys Lys Arg Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Deu Thr Gln Lys Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr Gln Lys Cys Gly Ile Asp Val Thr Val Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro 1\85 Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Qlu Leu Thr Lys

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys

35à

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser 370 380

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser 385 390 400

Leu Ser Leu Ser Pro Gly
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Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro Cys Pro Asp His Tyr 40 45

Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys teu Tyr Cys Ser Pro
50 55 60

Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu Cys Asn Arg Thr His
65 70 75 80

Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr Leu Glu Ile Glu Phe
85 90 95

Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe Gly Val Val Gln Ala 100 105 110

Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg Cys Pro Asp Gly Phe
115 120 125

Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys Arg Lys His Thr Asn 130 135 140

Cys Ser Val Phe Gly Leu Leu Thr Gln Lys Gly Asn Ala Thr His

Gly Gly Gly Gly Gly Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 180 185 190

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
195 200 205

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val 210 215 220

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val 225 230 235 240

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser 245 250 255

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu 260 265 270

Asn Gly Lys Glu Tyr Lys Cys Lys Wal Ser Asn Lys Ala Leu Pro Ala 275 280  $\downarrow$  285

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro 290 295 300

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln 305 310 315 320

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala 325 330 335

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
340 345 350

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu 355 360 365

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser 370 380

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Leu Ser Pro Gly

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|  | Met        | His<br>210 | Glu        | Ala        | Leu        | His        | Asn<br>215 | His        | Tyr        | Thr        | Gln        | Lys<br>220 | Ser        | Leu        | Ser        | Leu        |
|--|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
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|  | Glu        | Thr        | Ser        | His        | Gln<br>245 | Leu        | Leu        | Cys        | Asp        | Lys<br>250 | Cys        | Pro        | Pro        | Gly        | Thr<br>255 | Tyr        |
|  | Leu        | Lys        | Gln        | His<br>260 | Cys        | Thr        | Ala        | Lys        | Trp<br>265 | Lys        | Thr        | Val        | Cys        | Ala<br>270 | Pro        | Cys        |
|  | Pro        | Asp        | His<br>275 | Туг        | Tyr        | Thr        | Asp        | Ser<br>280 | Trp        | His        | Thr        | Ser        | Asp<br>285 | Glu        | Cys        | Leu        |
|  | Tyr        | Cys<br>290 | Ser        | Pro        | Val        | Cys        | Lys<br>295 | Glu        | Leu        | Gln        | Tyr        | Val<br>300 | Lys        | Gln        | Glu        | Cys        |
|  | Asn<br>305 | Arg        | Thr        | His        | Asn        | Arg<br>310 | Val        | Cys        | Glu        | Cys        | Lys<br>315 | Glu        | Gly        | Arg        | Tyr        | Leu<br>320 |
|  | Glu        | Ile        | Glu        | Phe        | Cys<br>325 | Leu        | Lys        | His        | Arg        | Ser<br>330 | Cys        | Pro        | Pro        | Gly        | Phe<br>335 | Gly        |
|  | Val        | Val        | Gln        | Ala<br>340 | Gly        | Thr        | Pro        | Glu        | Arg<br>345 | Asn        | Thr        | Val        | Cys        | Lys<br>350 | Arg        | Cys        |
|  | Pro        | Asp        | Gly<br>355 | Phe        | Phe        | Ser        | Asn        | Glu<br>360 | Thr        | Ser        | Ser        | Lys        | Ala<br>365 | Pro        | Cys        | Arg        |
|  | Lys        | His<br>370 | Thr        | Asn        | Cys        | Ser        | Val<br>375 | Phe        | Gly        | Leu        | Leu        | Leu<br>380 | Thr        | Gln        | Lys        | Gly        |
|  | Asn<br>385 | Ala        | Thr        | His        | Asp        | Asn<br>390 | Ile        | Cys        | Ser        | Gly        | Asn<br>395 | Ser        | Glu        | Ser        | Thr        | Gln<br>400 |

Lys